University of Pennsylvania Exploratory Center (P20) for Interdisciplinary Research

Human Pharmacogenomic Epidemiology

Stephen E. Kimmel, MD, MSCE

University of Pennsylvania School of Medicine

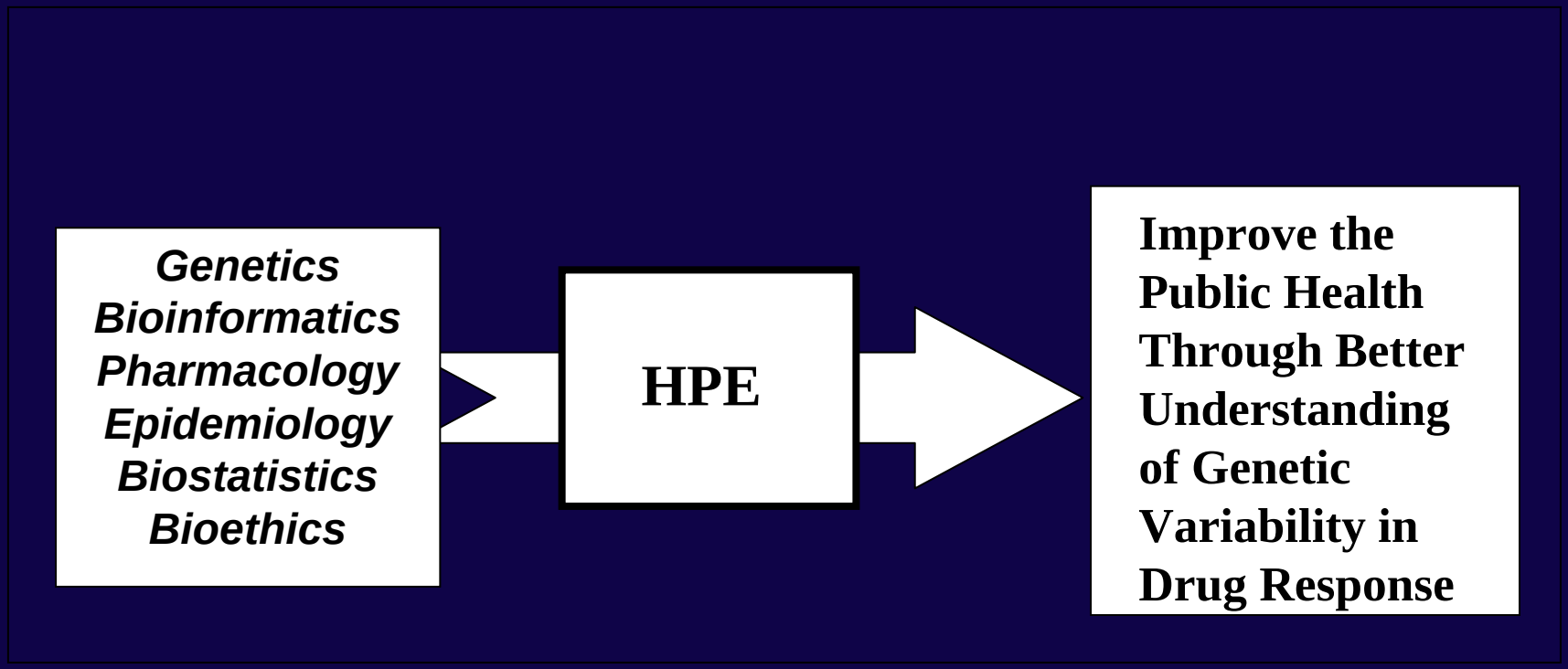
Overview

- **The Problem:**
  - **Genetic variability in the response to medications is a complex problem**
  - **Requires an interdisciplinary effort among**
    - **genetics**
    - **pharmacology**
    - **epidemiology**
    - **biostatistics**
    - **bioethics**
    - **bioinformatics**
  - **Together make up Human Pharmacogenomic Epidemiology (HPE)**

Barriers

- Scientific
  - e.g., false negatives, false positives
- Logistical
  - e.g., ensuring adequate sample size, measuring phenotype
- Intellectual
  - e.g., lack of appreciation of other disciplines, differences in scientific languages

The Goal


Genetics
Bioinformatics
Pharmacology
Epidemiology
Biostatistics
Bioethics
HPE
Improve the Public Health Through Better Understanding of Genetic Variability in Drug Response

The Team

- Steve Kimmel – epidemiology
- Tim Rebbeck – genetic epidemiology
- Steve Whitehead – pharmacology
- Rich Spielman – genetics/genomics
- David Roos – genomics/bioinformatics
- Hongzhe Li – statistical genetics
- Pamela Sankar – bioethics

Five Points to Cover

- Understanding each other's disciplines
- Evaluation techniques
- Team building
- Institutional support
- Management structure

Five Points to Cover

- **Understanding each other's disciplines**
- **Evaluation techniques**
- **Team building**
- **Institutional support**
- **Management structure**

Understanding Each Other's Disciplines

- Open discussions at monthly meetings
  - Each with a purpose
    - e.g., our 1st meeting:
      - What do you do?
      - How do you do it?
      - What do you need to do it better?
        - Led to a formal interdisciplinary survey (later)

Understanding Our Disciplines

- Development of internal RFA for pilot grants
  - Develop requirements to judge grants from different disciplines
  - Need for all to understand strengths and limitations of different approaches to solving problems
  - By requiring that grants focus on our barriers, forced us to confront and discuss those barriers
- Language building
  - Initially informally
  - Launched a formal study

"Facilitating Transdisciplinarity In HPE"

- To identify related and divergent assumptions about:
  - The function of participant's field relative to others
  - Barriers among fields
  - Common ground that already exists among fields
  - Changes necessary to sustain interdisciplinary work

"Facilitating Transdisciplinarity In HPE"

- 20 researchers from across the disciplines
- Written survey & face-to-face interviews
- Interview included asking participants to draw 2 "idea webs"
  - 1st shows existing relations among fields
  - 2nd web shows arrangement of fields required for interdisciplinary HPE

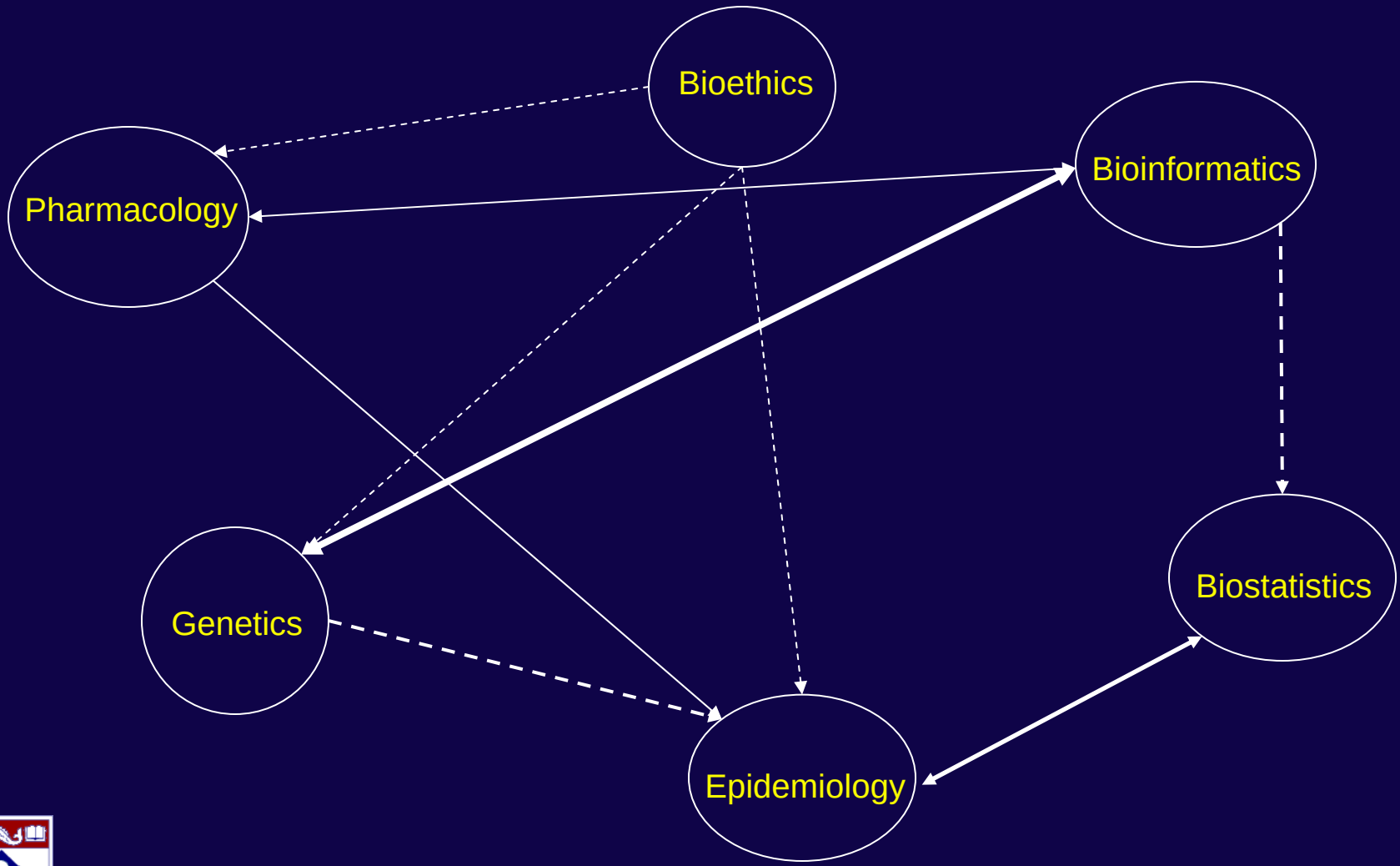
Degree of Mutual Understanding

	Understand Objectives	Understand Methods	Understand Language	Have Attended Colloquium	Have Many Friends	Share Goals	Use Their Results
Bioethics							
Bio-Informatics							
Bio-Statistics							
Epi-demiology							
Genetics							
Pharma-cology							

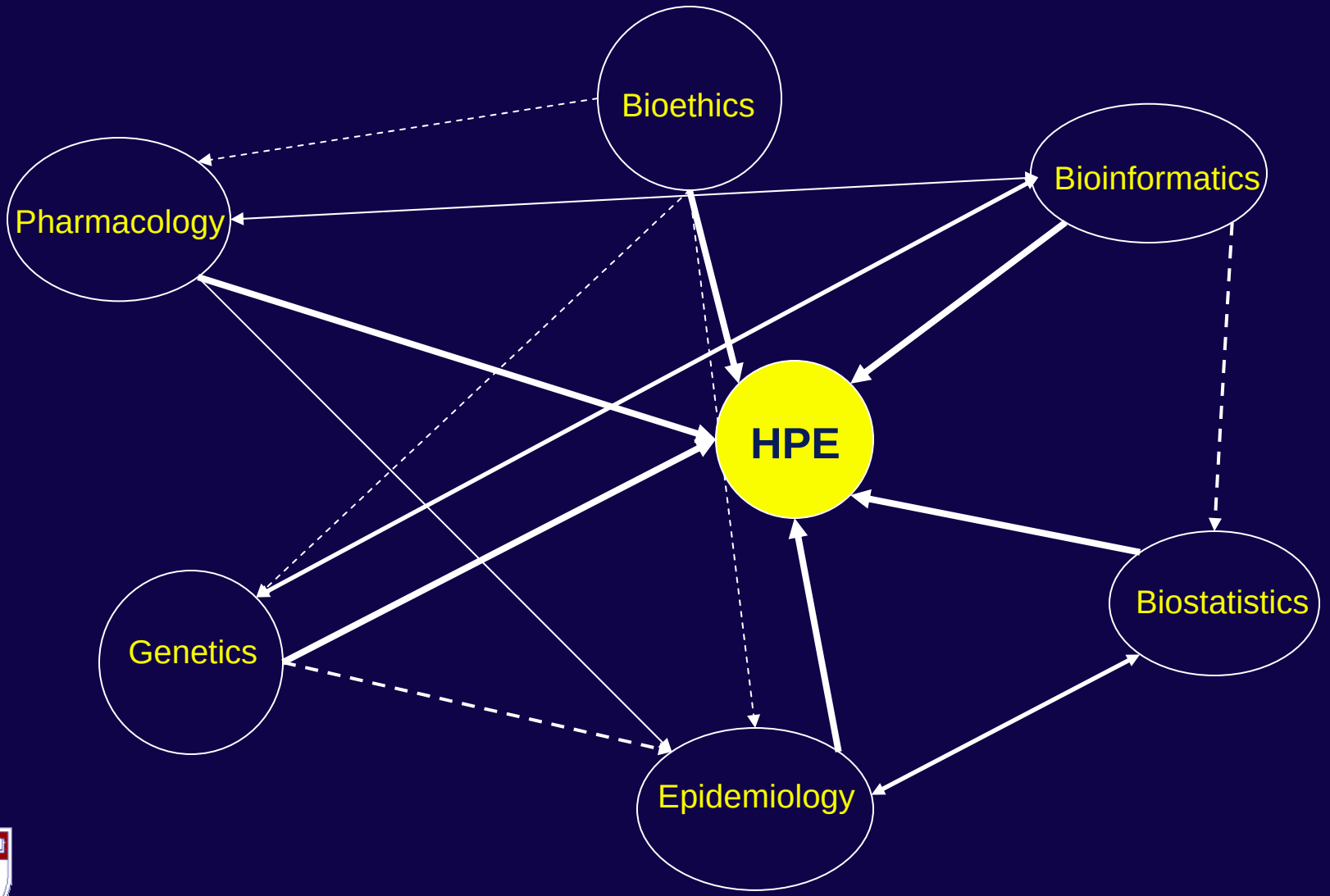
solid white = 0%

solid black=75-100%

Current relationships among HPE component fields (Bioinformatician viewpoint)



What happens when HPE is introduced (Bioinformatician viewpoint)



Five Points to Cover

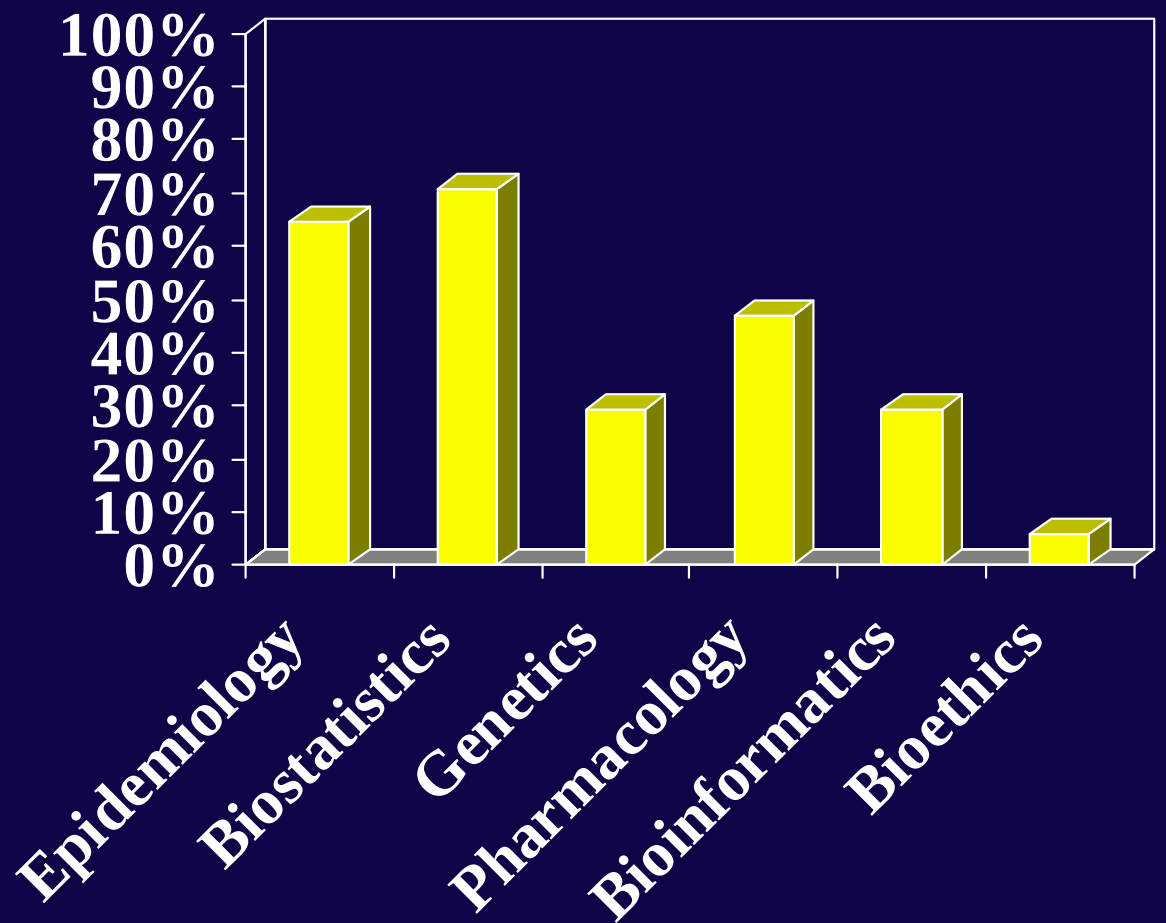
- Understanding each other's disciplines
- **Evaluation techniques**
- Team building
- Institutional support
- Management structure

Evaluation techniques

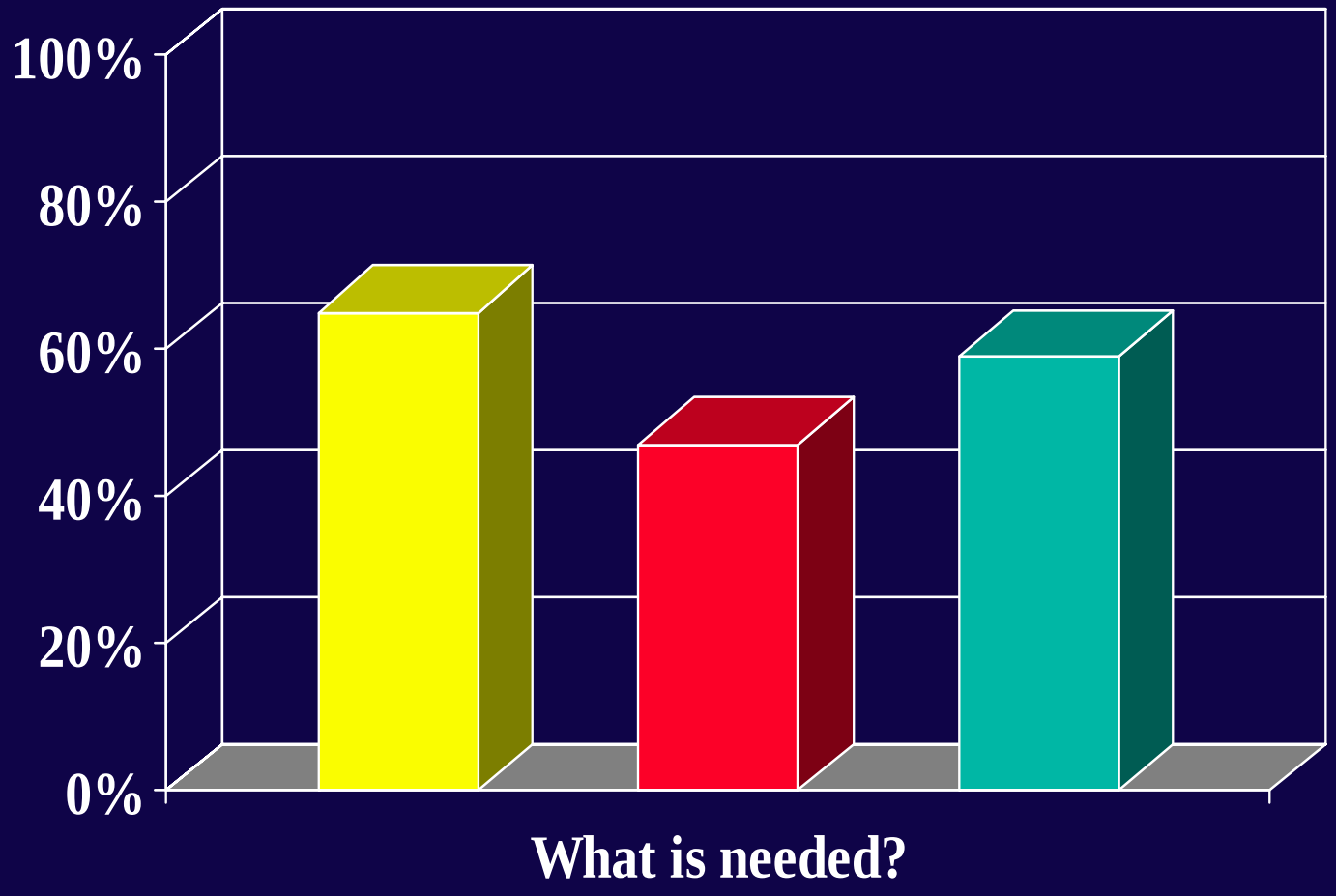
- Formal
  - Formal Study: “Facilitating Transdisciplinarity In HPE”
  - Pilot reports
  - Survey across-disciplines
    - Asked the same questions we asked of ourselves
      - This allowed us to evaluate our own assessments and viewpoints
    - A major finding: people didn’t know and/or understand the resources available within other’s disciplines

Interdisciplinary Survey

With Whom Do You Collaborate?



What is Needed to Improve Your Interdisciplinary Work?



Survey Text

- Asked people to list the barriers they face (within our 3 groups of pre-identified barriers) to improving their interdisciplinary research

Formal Survey: Some Examples

- Need to “understand the services offered”
  - Presentations of core services to the research community and posted on our website
- “Limited opportunities for interaction among individuals interested in pharmacogenetics”
  - Interdisciplinary Research retreat
  - Other meetings

Formal Survey: Some Examples (cont)

- "There is a clear barrier between geneticists' way of thinking (heritability) and epidemiologists' way of thinking about risk factors and populations."
  - Funded for pilot to develop interdisciplinary educational content
    - e.g., "Expert cross-talk" and "Barriers I face" seminars

Evaluation techniques

- **Informal**
  - **Monitoring response of the research community**
  - **Monitoring of interest**
  - **“Name recognition”**

Five Points to Cover

- Understanding each other's disciplines
- Evaluation techniques
- **Team building**
- Institutional support
- Management structure

Team building

- Most of us knew each other beforehand
  - Or so we thought!
- We have all developed a much better understanding of each others' point of view, scientific language, and core values
  - How?

Team building – how?

- Monthly meetings
- Working together
  - Developing and analyzing survey results
  - Development of RFA for pilot grants
  - Planning, executing, and analyzing retreat
  - Planning seminars, speakers, Visiting Scholars

Team building

- Change in membership
  - Hongzhe Li for Jesse Berlin in biostats
  - Pamela Sankar for Art Caplan in bioethics
  - Clearly due to the interdisciplinary nature of our work
- Additions
  - e.g., psychiatry, genetics, biostatistics, epidemiology, neurology

Five Points to Cover

- Understanding each other's disciplines
- Evaluation techniques
- Team building
- **Institutional support**
- Management structure

Institutional Support

- Penn sponsored our P20 Interdisciplinary Research Retreat
- Support for Visiting Scholars from across the disciplines
- New space provided for our burgeoning statistical and genetic epidemiology groups
- Part-time sabbatical

Institutional Stance Toward Interdisciplinary Research

- Some examples
  - 3 new interdisciplinary Institutes
  - Multiple new initiatives to develop interdisciplinary training
    - P20 providing support for cross-training
  - Interdisciplinary Pilot Project Program

Five Points to Cover

- Understanding each other's disciplines
- Evaluation techniques
- Team building
- Institutional support
- Management structure

Management Structure

- Steering Committee with a representative from each discipline
- All decisions are made as a group
  - Pilot funding as an example
- Clear goals

Future Plans

- Feedback results of studies to the research community
- Continue to plan activities to reduce barriers identified
  - Interdisciplinary seminar series
  - Increase understanding of and access to resources within each discipline
  - Fund 2nd round of pilot studies
  - Continue to fund cross-training

HPE Website :

http://www.cceb.upenn.edu/hpe